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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,950	09/08/2006	**Helen Francis-Lang**	05-967-D5	5893

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EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,950	FRANCIS-LANG ET AL.	
	Examiner	Art Unit	
	Richard Schnizer	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6,8-12 and 16-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6, 8-12, and 16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/24/0; 8/16/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner and art unit handling this application have changed. Please direct further correspondence to Richard Schnizer (AU 1635), whose contact information is given at the end of this Office Action.

An amendment was received and entered on 4/27/09. Applicant's election with traverse of Group II claims 1-12 and 16-19, drawn to methods of identifying a candidate beta catenin pathway modulating agent in a system comprising PRKC nucleic acids, and the species of a nucleic acid antisense oligomer and a cell proliferation assay, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant asserts that the elected invention reads on claims 1-12 and 16-19. However, claim 4 is drawn to a small molecule agent, not to an antisense oligomer; claim 5 is drawn to a kinase assay system, not to a cell proliferation assay system; and claim 7 is drawn to an antibody test agent, not to an antisense oligomer. Accordingly claims 4, 5, and 7 do not read on the elected invention.

Claims 4, 5, 7, 13-15, and 20-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/27/09.

Claims 1-3, 6, 8-12, and 16-19 are under consideration.

Priority

This Application is the National Stage of PCT/US2004/26361, filed 8/13/2004, and claims priority to UD provisional application 60/495,172, filed 8/14/2003. The claims as currently pending are drawn to methods utilizing an assay system comprising a PRKC nucleic acid. In view of the specification as filed the term "PRKC" is taken to be synonymous with "PKC", or protein kinase C. See page 3, lines 1 and 2. Thus the claims embrace the entire genus of protein kinase C nucleic acids. The PKC family comprises a wide variety of isoforms, including alpha, $beta_I$, $beta_{II}$, delta, gamma, eta, omega, lambda, iota, and zeta. Provisional application 60/495,172 supports only PKC zeta and PKC iota. Because the instant claims read on PKC nucleic acids that are not supported in the priority document 60/495,172, such as PKC alpha, they are not entitled to the priority date of 60/495,172. The effective filing date of the instant claims is considered to be 8/13/2004, the filing date of PCT/US2004/26361.

Drawings

The application as filed contained no drawings.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is indefinite because it recites "the assay" without proper antecedent basis. Claim 5 depends from claim 4, which recites an assay system and a screening assay. It is unclear to which assay "the assay" refers.

Claim 10 is indefinite because it is unclear what is intended by "PMO". "PMO" is an acronym recognized by those of ordinary skill as an abbreviation of phosphorodiamidate morpholino. However, the instant specification at page 18 indicates that this acronym means "phosphorothioate morpholino". The specification then refers to several references to provide guidance as to how to make and use PMOs. None of the references supports the term "phosphorothioate morpholino", and the 5,235,033 and 5,378,841 patents, and the Summerton (1997) article, disclose that morpholino oligonucleotides generally have a phosphorodiamidate linkage. Because this is different from the non-art-recognized definition at specification page 18, it is unclear what is meant by PMO in claim 10.

Claim 16 is indefinite in that the metes and bounds of "additional steps" are unclear. The additional steps begin with step e) whereas claim 1 only recites steps a)-c). Therefore, claim 16 is missing step d).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6, 8, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Murray et al (J. Biol. Chem. 268(11): 15847-15853, 1993).

Murray taught a proliferation based assay wherein cells that expressed PKC alpha, $beta_{II}$, and zeta were treated with antisense against PKC $beta_{II}$. The proliferation phenotype of the cells was assayed. See abstract. Note that the active method steps of the rejected claims provide absolutely no nexus between beta catenin, PRKC, and the candidate agents, such that these claims are anticipated by any prior art method in which an antisense oligonucleotide is added to cells in a proliferation assay, wherein the cells comprise PKC nucleic acids. Thus Murray anticipates the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 6, 8-12, and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Costa et al (WO 03/052068, of record) as evidenced by Rennecke et

al (Eur. J. Biochem. 242: 428-432, 1996) and Wetsel et al (J Cell Biol. 117(1): 1221-133, 1992).

Costa taught methods of identifying a candidate beta-catenin pathway modulating agent, said method comprising the steps of:

(a) providing an assay system comprising a modulator of beta catenin nucleic acid;

(b) contacting the assay system with a test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and

(c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate beta-catenin pathway modulating agent. See claim 1.

The limitations of instant claims 6, 8-12 and 16-19 are present in claims 6, 8-12 and 16-19 of Costa, in particular Costa taught a PMO antisense oligomer as a test agent nucleic acid modulator, and a cell proliferation assay system (see claims 6 and 10).

Costa did not explicitly disclose a system comprising a PKRC nucleic acid, but did suggest using mammalian cell lines in the assay systems (see page 27, lines 1 and 2), and mammalian cell lines are known to comprise PKC family genes, i.e. genes encoding PKC alpha, $beta_I$, $beta_{II}$, delta, gamma, eta, omega, lambda, iota, and zeta. A search of the prior art did not reveal any mammalian cell line in which every copy of every PKC isozyme had been deleted, (i.e. the search did not reveal any mammalian cell line that lacked a PKC nucleic acid). Moreover, the art shows that PKC enzymes are ubiquitous in mammalian cells (see e.g. Rennecke who indicated that PKC mu was

present in all cells and tissues (abstract), or Wetsel who indicated that PKC alpha was present in all tissues (abstract)). Thus, absent specific guidance to delete all PKC isoform genes from a cell's genome, it would have been obvious for one of ordinary skill in the art at the time of the invention to use in the method of Costa a cell line comprising at least one PKC nucleic acid. Similarly, as evidenced by Rennecke and Wetsel, absent guidance to eliminate expression of all PKC isoforms, it would have been obvious to use a cell line that comprised at least one PKC isoform. No such guidance is present in Costa, therefore the invention as a whole was prima facie obvious.

Claims 1, 2, 6, and 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murray et al (J. Biol. Chem. 268(11): 15847-15853, 1993) in view of Summerton et al (Antisense & Nucleic acid Drug Dev. 7: 187-195, 1997).

Murray taught a proliferation based assay wherein cells that expressed PKC alpha, $beta_{II}$, and zeta were treated with antisense deoxyribooligonucleotides against PKC $beta_{II}$. The proliferation phenotype of the cells was assayed. See abstract and page 15848, left column, fourth full paragraph. Note that the active method steps of the rejected claims provide absolutely no nexus between beta catenin, PRKC, and the candidate agents, such that these claims are anticipated by any prior art method in which an antisense oligonucleotide is added to cells in a proliferation assay, wherein the cells comprise PKC nucleic acids. Thus Murray anticipates and renders obvious claims 1, 2, 6, 8, and 9.

Murray did not teach a PMO oligonucleotide.

Summerton taught that phosphorodiamidate morpholino (PMO) oligonucleotides overcome problems associated with first generation antisense chemistries, provide high and predictable activity in cells, and exhibit little or no nonantisense activity, afford good water solubility, are immune to nucleases. See abstract. Therefore one of ordinary skill in the art at the time of the invention would have found it obvious and would have been motivated to substitute PMO oligonucleotides for the standard oligonucleotide chemistry of Murray, in order to obtain the perceived advantages of PMO oligonucleotides.

Claims 1, 2, 6, 8, 9, 11, 12, 16, 18, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murray et al (J. Cell Biol. 145(4): 699-711, 1999) in view of Murray et al (J. Biol. Chem. 268(11): 15847-15853, 1993).

Murray (1999) taught that overexpression of PKC $beta_{II}$ induced colonic hyperproliferation and increased sensitivity to colon carcinogenesis in a transgenic mouse model. Transgenic PKC $beta_{II}$ mice exhibited elevated colonic beta catenin levels and glycogen synthase 3beta activity indicating that PKC $beta_{II}$ stimulates the Wnt/APC/beta catenin proliferative signaling pathway in vivo.

Murray did not teach treatment of cells with antisense against PKC $beta_{II}$.

Murray (1993) studied the role of PKC $beta_{II}$ on cell proliferation in K562 erythroleukemic cells. Murray showed that proliferating cells expressed PKC $beta_{II}$, and that cells that overexpressed PKC $beta_{II}$ were less sensitive to cytostatic effects normally induced by phorbol myristate acetate (PMA). Murray also showed that proliferation of PMA-withdrawn cells can be inhibited by treatment with PKC $beta_{II}$

antisense, thereby confirming the role of PKC $beta_{II}$ in cellular proliferation. See abstract.

It would have been obvious to one of ordinary skill in the art at the time of the invention to have used the antisense of Murray (1993) to treat the colonic cells of the mouse of Murray (1999). One would have been motivated to do so, as in the case of Murray (1993), in order to confirm that the activity of PKC $beta_{II}$ in those cells was responsible for the observed phenotype (colonic hyperproliferation, increased sensitivity to colon carcinogenesis, and elevated colonic beta catenin levels and glycogen synthase 3beta activity). In so doing, one would have taken the antisense agent identified in a method anticipating the method of claims 1, 2, 6, 8, and 9 (Murray (1993)), and applied it in a second, animal-based model system in which the animal misexpressed beta catenin. Note that the specification at paragraph 81 indicates that "defective beta catenin function" includes beta catenin overexpression or underexpression relative to wild type. So, the animal model of Murray (1999), which overexpresses beta catenin, shows defective beta catenin function as defined by the specification. Thus the invention as a whole was prima facie obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the

hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, James (Doug) Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

/Richard Schnizer/
Primary Examiner, Art Unit 1635